

ABSTRACT

The present invention relates to novel chemistries which allow for heretofore unobtainable substituted tetracycline compounds which exhibit significant 5 activity in tetracycline responsive states. The methods disclosed herein utilize reactive tetracycline-based precursor compounds, reactive organic substituent precursors and transition metal catalysts under conditions such that a tetracycline compound substituted with the desired organic substituent is formed. In one embodiment of the invention, a substituted tetracycline compound may be prepared by combining a reactive 10 tetracycline-based precursor compound such as an arene tetracycline diazonium salt, and a reactive organic substituent precursor, e.g., alkenes, substituted alkenes, vinyl monomers, aromatics and heteroaromatics, in the presence of a transition metal catalyst, such as palladium chloride, under conditions such that a tetracycline compound substituted with the organic substituent is formed. Such compounds may optionally act 15 as intermediates for making other compounds, e.g., hydrogenation of unsaturated groups on the substituent.